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REMARKS

I. Status of the Application

Claims 1, 3-8 and 10-13 are presently pending in the Application. Claims 1, 4, 6, 8 and 11 stand rejected under 35 U.S.C. §102(b) over JP 63236847 ("Cho"). Claims 1, 3-8 and 10-13 stand rejected under the judicially created doctrine of obvious-type double patenting over US Patent No. 6,074,662.

The above amendments to the specification are being made to correct a previously unidentified typographical error in the priority information as well as to update the status of the application from which the present application claims priority. The Examiner identified the typo in the office action dated March 29, 2001 (paper no. 11). Applicant submits that the typographical error was made in good faith and that no new matter will be added to the application upon entry of this amendment. In addition, applicant is providing the Examiner herewith a copy of the declaration from the parent application 08/698,475, which may not have been submitted with the application as filed. Applicant submits that since this is a continuation application, no new declaration is required to be executed by the inventor.

Applicant has amended Claim 11 to correct a self-evident error. Support for this amendment is found at page 5, line 11. Applicant submits that the error was made in good faith and that entry of this amendment will not necessitate a new search to be made by the Examiner.

Applicant has requested entry of new Claims 14-21 on the basis that the Examiner has not rejected Claims 3, 5, 7, 10, 12 and 13 under § 102(b) over Cho and, accordingly, are each patentable upon traversing any outstanding rejection. Claims 3, 5, 7, 10, 12 and 13 are presently rejected only under the obvious-type double patenting rejection, which is being overcome by filing a terminal disclaimer herewith. Applicant believes that new Claims 14-21 are patentable

and do not necessitate a new search by the Examiner because the only new independent claims presented, Claims 14 and 18, both incorporate the limitation of Claim 7, which is patentable. In view of Applicant filing a terminal disclaimer herewith, Applicant respectfully requests allowance of new Claims 14-21 at this time.

II. Claims 1, 4, 6, 8, and 11 Are Patentable Over Cho

Claims 1, 4, 6, 8, and 11 stand rejected over Cho. The Examiner maintains his assertion that Cho teaches each and every element of Applicant's claimed subject matter. Applicant respectfully traverses the rejection.

Claim 1 is directed to a device for delivering a therapeutic agent to an animal having a carrier with a negatively charged surface and an effective antimicrobial dose of one or more cationic antimicrobial substances in a saliva soluble form. The negatively charged surface serves to retain the one or more cationic antimicrobial substances to the carrier. An alkali metal salt is also included in the device in an amount effective to promote the solubility of the cationic antimicrobial substance in saliva.

Applicant believes that Cho in its entirety does not disclose each and every element of Claim 1 and all dependent claims therefrom. For example, Cho fails to teach a carrier *with a negatively charged surface*. The Examiner asserted on page 2 in the previous office action (paper no. 15) that the use of cetyl pyridinium chloride with the negative carrier, gelatin, anticipates Claim 1. Applicant, however, respectfully disagrees with the Examiner that Cho, by its generic reference to gelatin, necessarily discloses a carrier with a negatively charged surface. Applicant believes that the generic reference to "gelatin" is not necessarily a disclosure of a carrier with a negatively charged surface because one would not expect gelatin to be negatively

charged without some positive affirmation to that effect. This is because gelatin is generally known as denatured collagen, which has a distinctive amino acid composition in which about one third of its residues are glycine and up to 30% of the remaining residues are either proline or 4-hydroxyproline. Donald Voet and Judith Voet, Biochemistry, 160 (John Wiley & Sons 1990). See Attachment A. Since glycine, proline and 4-hydroxyproline are charge neutral amino acids, it does not follow that gelatin necessarily has a negatively charged surface without there also being negatively charged moieties present. Cho makes no positive affirmation that the "gelatin" disclosed has any charge or contains any charged moieties. Thus, the mere teaching of "gelatin" is an inadequate disclosure of a carrier with a negatively charged surface. Accordingly, Applicant believes that the disclosure of "gelatin" in Cho fails to anticipate a carrier with a negatively charged surface as defined by Claim 1.

Further, Cho fails to disclose an alkali metal salt *to promote the solubility of the cationic antimicrobial substance* in the saliva as defined by all pending claims. A purpose of the alkali metal salt in the claimed device is explained on page 4, line 25 to page 5, line 3 of the Application:

> In a preferred embodiment, the cation is rapidly solubilized in the saliva of the oral cavity when the cation is combined with or deposited on the chew in the presence of an alkali metal salt such as sodium gluconate. It has unexpectedly been found that **the presence of the alkali metal salt effectively prevents the cationic compound from precipitating or otherwise adhering to the proteinaceous carrier**, thus rendering it readily soluble in saliva during the chewing cycle. (Emphasis added)

Alternatively, Cho does not disclose using an alkali metal salt to promote the solubility of the cationic antimicrobial substance. In fact, Cho never mentions why an alkali metal salt is used as a component in the composition of Embodiment 2. On page 2 of the previous office action (paper no. 15), the Examiner asserted that the alkali salt of saccharine disclosed in Cho was

"clearly a replacement for the sugar in embodiment one suitable for those dogs wishing to reduce caloric intake." Cho discloses on page 4, paragraph 2 that sugar is used in the composition to increase the chewability of the capsule. It thus follows from the Examiner's assertion that the alkali metal salt disclosed in Cho is not present to promote the solubility of the cationic antimicrobial substance, but rather to increase the chewability of the capsule. This is abundantly clear considering that the composite in Embodiment 2, which makes the only reference to an alkali metal salt, does not further comprise a cationic antimicrobial substance. In this regard, it is also apparent that the alkali metal salt in Cho does not inherently disclose an alkali metal salt to promote the solubility of the cationic antimicrobial substance. Thus, Applicant believes that all pending claims are patentable over Cho and removal of the present rejection is respectfully requested at this time.

III. Claims 1, 3-8 and 10-13 Are Patentable over U.S. Patent 6,074,662

Claims 1, 3-8 and 10-13 stand rejected under the judicially created doctrine of obvious-type double patenting over Claim 1 of the '662 patent. In view of the amendment above correcting priority of the present Application to the '662 patent, which claims priority to Provisional application No. 60/002,345, Applicant deems this rejection overcome by submitting a terminal disclaimer herewith. Thus, all pending claims are patentable over the '662 patent.

IV. Conclusion

Having addressed all outstanding issues, Applicant respectfully requests reconsideration and allowance of Claims 1, 3-8, 10-13 and 14-21.

Respectfully submitted,

Dated: December 2, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Please replace the paragraph beginning at page 1, line 7 with the following paragraph:

This application is a continuation of U.S. application Serial No. [08/689,475] 08/698,475, filed August 15, 1996 now U.S. Pat. No. 6,074,662 that claims priority from U.S. provisional application Serial No. 60/002,345, filed August 15, 1995. Both of these related applications are hereby incorporated herein by reference.

In the Claims:

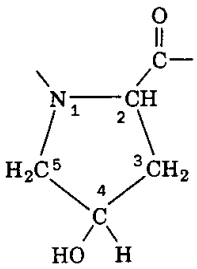
Please amend claim 11 as follows:

11. (Twice Amended) A method according to claim 8, wherein the one or more cationic antimicrobial substances are selected from the group consisting of chlorhexidine diacetate, chlorhexidine digluconate, cetylpyridinium chloride, domiphen bromide, [benzalonium] benzalkonium chloride, benzethonium chloride, and alexidene.

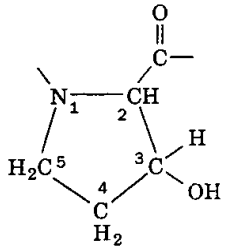
major stress-bearing component of **connective tissues** such as bone, teeth, cartilage, tendon, ligament, and the fibrous matrices of skin and blood vessels. Collagen occurs in virtually every tissue.

A single molecule of Type I collagen has a molecular mass of ~285 kD, a width of ~14 Å, and a length of ~3000 Å. It is composed of three polypeptide chains. Mammals have at least 17 genetically distinct polypeptide chains comprising 10 collagen variants that occur in different tissues of the same individual. The most prominant of these are listed in Table 7-2.

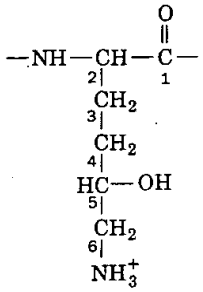
Collagen has a distinctive amino acid composition: Nearly one third of its residues are Gly; another 15 to 30% of its residues are Pro and ***4-hydroxyproline (Hyp).***



4-Hydroxyprolyl residue (Hyp)



3-Hydroxyprolyl residue



5-Hydroxylysyl residue (Hyl)

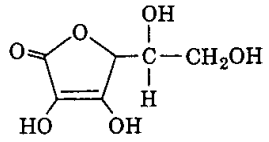
3-Hydroxyproline and **5-hydroxylysine (Hyl)** also occur in collagen but in smaller amounts. Radioactive labeling experiments have established that these nonstandard hydroxylated amino acids are not incorporated into collagen during polypeptide synthesis: If ^{14}C-labeled 4-hydroxyproline is administered to a rat, the collagen synthesized is not radioactive, whereas radioactive collagen is produced if the rat is fed ^{14}C-labeled proline. The hydroxylated residues appear after the collagen polypeptides are synthesized, when certain Pro residues are converted to Hyp in a reaction catalyzed by the enzyme **prolyl hydroxylase.**

Hyp confers stability upon collagen, probably through intramolecular hydrogen bonds that may involve bridging water molecules. If, for example, collagen is synthesized under conditions that inactivate prolyl hydroxylase, it loses its native conformation (denatures) at 24°C, whereas normal collagen denatures at 39°C (denatured collagen is known as **gelatin**). Prolyl hydroxylase requires **ascorbic acid (vitamin C)**

Table 7-2
The Most Abundant Types of Collagen

Type	Chain Composition	Distribution
I	$[\alpha 1(I)]_2\alpha 2(I)$	Skin, bone, tendon, blood vessels, cornea
II	$[\alpha 1(II)]_3$	Cartilage, intervertebral disk
III	$[\alpha 1(III)]_3$	Blood vessels, fetal skin

Source: Eyre, D. R., *Science* **207**, 1316 (1980).



Ascorbic acid (Vitamin C)

to maintain its enzymatic activity. In the vitamin C deficiency disease **scurvy**, the collagen synthesized cannot form fibers properly. This results in the skin lesions, blood vessel fragility, and poor wound healing that are symptomatic of scurvy.

The amino acid sequence of bovine collagen α1(I), which is similar to that of other collagens, consists of monotonously repeating triplets of sequence Gly-X-Y over a continuous 1011-residue stretch of its 1042-residue polypeptide chain (Fig. 7-30). Here X is often Pro and Y is often

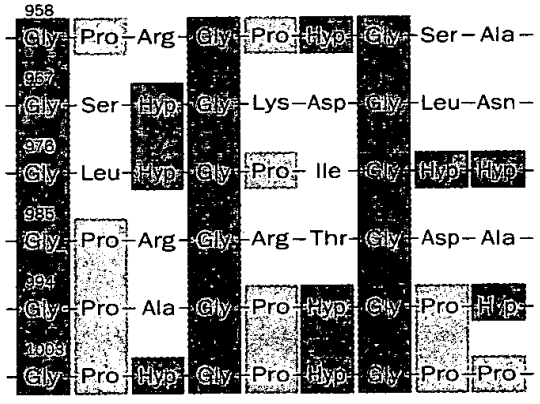


Figure 7-30
The amino acid sequence at the C-terminal end of the triple helical region of the bovine α1(I) collagen chain. Note the repeating triplets Gly-X-Y, where X is often Pro and Y is often Hyp. Here, Hyp* represents 3-hydroxy Pro. [From Bornstein, P. and Traub, W., *in* Neurath, H. and Hill, R. L. (Eds.), *The Proteins* (3rd ed.), Vol. 4 *p.* 483, Academic Press (1979).]